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Polymer drug matrix loading in micro-containers using hot punching

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We present here, a new technique for loading of large arrays of SU-8 micro-containers for oral drug delivery. The SU-8 containers are fabricated using photolithography and then hot punching in a spin coated drug layer is used to fill them. This process of filling micro-containers is a 1-step process that is fast and clean, and potentially enables high volume production.

Recent advancement in microtechnology has led to the development of new drug delivery devices. One such device is microcontainer that can be used for oral drug delivery [1]. Microcontainers are able to protect drug from degradation in the gastro-intestinal tract. Furthermore, they provide one-directional drug release at the site of absorption and can thereby enhance the bioavailability of drugs. Because of their size, they are needed in large numbers for every dosage. It is difficult and time consuming to fill arrays of such small containers. To date, filling has been done by inkjet printing and micro spotting [2]. These are slow serial processes for drugs in liquid form. Another method that has been introduced recently is using hydrogels. However, this approach requires multiple steps of deposition, crosslinking, swelling etc. [2][3][4].

In this work, SU-8 micro-containers are fabricated on wafer scale using a two-step photolithography [5]. These micro-containers are 300 microns in diameter and 100 microns in height (Fig. 1(a), Fig. 2). The containers are fabricated on fluorocarbon coating to aid their final release from the Si substrate. To fill these micro-containers, we developed a hot punching technique which is illustrated in Fig. 1. First, the substrate is prepared by spin coating a PDMS layer of 50 μm on a Si wafer. Then around 60 μm thick layer of Polycaprolactone (PCL) and Furosemide solution is spin coated on the PDMS (Fig. 1(b)). After that the sample is embossed with SU-8 containers as a stamp for 15 min at a temperature of 60°C and a pressure of 1.9 MPa [4] (Fig. 1(c)). The viscoelastic under layer of PDMS deforms against the SU-8 container stamp and pushes the polymer into the cavities of the container. Due to this enhanced deformation, the residual layer is broken and the polymer-drug matrices are punched out of the spin coated film (Fig. 1(d)) [6]. Finally the SU-8 containers are demolded and the punched out drug-polymer matrices remain in the container cavity. Using this technique, each container is filled individually and there is no residual layer connecting the drug matrix that needs to be removed after the filling process (Fig. 3). Once the containers are filled using hot punching, they can be scraped off the Teflon coated Si wafer for drug release tests.

Preliminary in vitro dissolution drug release tests were performed on the spin-coated drug matrix (Fig. 1(b)) exposed to identical heat and pressure conditions as for the final devices. Fig. 4 shows that more than 95% of the furosemide is released within the first 30 minutes.

We have shown that it is easy to integrate filling of micro containers as part of the fabrication. In future we plan to do release tests on the final devices and also animal tests, filled with different drugs.

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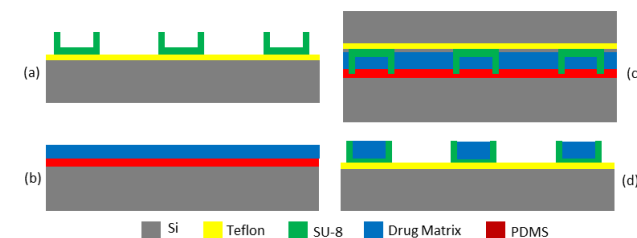


Fig 1. Hot punching of polymer matrix: SU-8 micro-containers (a); Spin coating PDMS and PCL-drug matrix layers on Si (b); Hot punching (c); Demolding, SU-8 containers with polymer drug matrix.

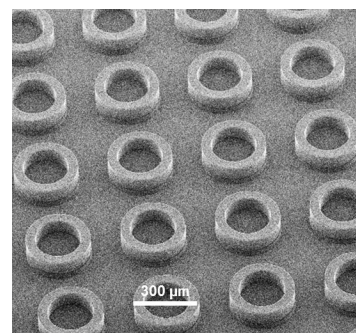


Fig.2. SU-8 micro-containers before hot punching.

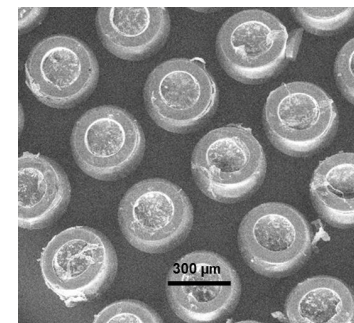


Fig.3. SU-8 micro-containers loaded with polymer matrix after hot punching.

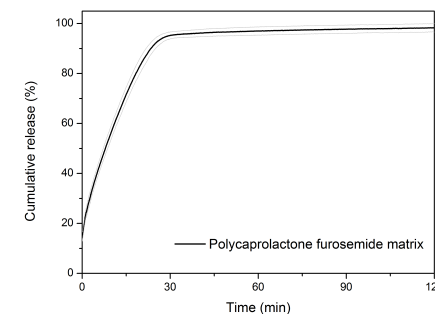


Fig.4. Release curve of PCL and furosemide matrix